Amendments to the Specification:

Please replace the paragraph beginning on page 1, line 4 with the following amended paragraph:

This application is a continuation-in-part of U.S. Patent Application No. 09/293,557 filed April 15, 1999, now U.S. Patent No. 6,251,382 which claims the benefit of priority from U.S. Patent Provisional Application Serial No. 60/082,105 filed April 17, 1998, the contents of each of which are incorporated herein by reference.

Please replace the paragraph beginning on page 1, line 14 with the following amended paragraph:

Over the years, several methods of administering biologically-effective materials to mammals have been proposed. Many medicinal agents are available as water-soluble salts and can be included in pharmaceutical formulations relatively easily. Problems arise when the desired medicinal agent is either insoluble in aqueous fluids or is rapidly degraded ~~in vivo~~ *in vivo*. Alkaloids are often especially difficult to solubilize.

Please replace the paragraph beginning on page 1, line 20 with the following amended paragraph:

One way to solubilize medicinal agents is to include them as a part of a soluble prodrug. Prodrugs include chemical derivatives of a biologically-active parent compound which, upon administration, eventually liberate the parent compound ~~in vivo~~ *in vivo*. Prodrugs allow the artisan to modify the onset and/or duration of action of an agent ~~in vivo~~ *in vivo* and can modify the transportation, distribution or solubility of a drug in the body. Furthermore, prodrug formulations often reduce the toxicity and/or otherwise overcome difficulties encountered when administering pharmaceutical preparations. Typical examples of prodrugs include organic phosphates or esters of alcohols or thioalcohols. See ~~Remington's Pharmaceutical Sciences~~ *Remington's Pharmaceutical Sciences*, 16th Ed., A. Osol, Ed. (1980), the disclosure of which is incorporated by reference herein.

Please replace the paragraph beginning on page 2, line 13 with the following amended paragraph:

Incorporating a polymer as part of a prodrug system has been suggested to increase the circulating life of a drug. However, it has been determined that when only one or two polymers of less than about 10,000 daltons each are conjugated to certain biologically active substances such as alkaloid compounds, the resulting conjugates are rapidly eliminated ~~in vivo~~ *in vivo*, especially if a somewhat hydrolysis-resistant linkage is used. In fact, such conjugates are so rapidly cleared from the body that even if a hydrolysis-prone ester linkage is used, not enough of the parent molecule is regenerated ~~in vivo~~ *in vivo* to be therapeutic.

Please replace the paragraph beginning on page 4, line 17 with the following amended paragraph:

In preferred aspects of the above embodiment,

~~R_1~~ R_{31} is preferably a PEG residue;

~~Y_1~~ Y_{11} and ~~Y_2~~ Y_{12} are both O;

~~R_2-R_{10}~~ R_{22}-R_{40}, R_{50}, and R_{51} are each hydrogen or a C_{1-4} alkyl;

a and *b* are each 1;

y_1 and y_2 are both one; and

D_1 and D_2 are both residues of either a hydroxyl- or amine-containing moiety such as one having biological activity as defined herein.

Please replace the paragraph beginning on page 10, line 15 with the following amended paragraph:

For purposes of illustration, a general formula (I) is provided:

(I) ~~$(D-)_n$-M-$(R)_m$~~ $(D-)_n$-M-$(L_1)_m$

wherein:

(m) and *(n)* are positive integers, preferably from about 1 to about 6 each;

D is a residue of a biologically active moiety;

M is a multifunctional linker/spacer moiety; and

R_1 is a polymer residue.

Please replace the paragraph beginning on page 21, line 4 with the following amended paragraph:

As stated above, ~~R~~ R_1 is a polymeric residue which is preferably substantially non-antigenic. Suitable examples of such polymers include polyalkylene oxides such as polyethylene glycols. The general formula for PEG and its derivatives, ~~i.e.~~ is

$$A'\text{-}O\text{-}(CH_2CH_2O)_x\text{-}(CH_2)_{n3}\text{-}A$$

where *(x)* represents the degree of polymerization (i.e. from about 10 to about 2,300) or number of repeating units in the polymer chain and is dependent on the molecular weight of the polymer, *(n3)* is zero or a positive integer, (A) is a terminal or capping group such as an amino, carboxy, halo, OH, C_{1-6} alkyl, preferably methyl and (A') is the same as (A) or another (A) moiety. Also useful are polypropylene glycols, branched PEG derivatives such as those described in commonly-assigned U.S. Pat. No. 5,643,575, "star-PEG's" and multi-armed PEG's such as those described in Shearwater Polymers, Inc. catalog "Polyethylene Glycol Derivatives 1997-1998". The disclosure of each of the foregoing is incorporated herein by reference. It will be understood that the water-soluble polymer can be functionalized for attachment to the multifunctional moiety M herein. As an example, the PEG portion of the inventive compositions can be one of the following non-limiting compounds:

$-C(=Y)\text{-}(CH_2)_{n3}\text{-}O\text{-}(CH_2CH_2O)_x\text{-}A$, $-C(=Y)\text{-}Y\text{-}(CH_2)_{n3}\text{-}O\text{-}(CH_2CH_2O)_x\text{-}A$,

and $-C(=Y)\text{-}NR_6\text{-}(CH_2)_{n3}\text{-}O\text{-}(CH_2CH_2O)_x\text{-}A$,

where Y is O, S or NR2 and A, R_2 and R_6, *(n3)* and *(x)* are as defined above.